The Relationship between Water Concentrations and Individual Uptake of Chloroform: A Simulation Study

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We simulated the relationship between water chloroform concentrations and chloroform uptake in pregnant women to assess the potential extent of exposure measurement error in epidemiologic studies of the health effects of exposure to water disinfection by-products. Data from the literature were used to assign statistical distributions to swimming pool chloroform concentrations, frequency and duration of swimming, showering and bathing, and average tap water consumption. Measured increases in blood chloroform concentrations after these activities were used to estimate average uptake per microgram per liter chloroform in the water, per minute spent in the activity or per liter consumed. Given average tap water chloroform concentrations from a U.K. epidemiologic study, an average daily uptake over 90 days was simulated for 300,000 mothers. The correlation between simulated uptakes and home tap chloroform concentration was 0.6. Mothers who swam regularly received far greater doses than did nonswimmers. Results suggest there will be considerable attenuation in risk estimates and/or power loss in epidemiologic studies if the putative agent is chloroform. *Key words:* **activity patterns, chlorination, chloroform, disinfection by-products, measurement error.** *Environ Health Perspect* **111:688–694 (2003). doi:10.1289/ehp.5963 available via *http://dx.doi.org/* [Online 9 December 2002]**

Chloroform ($CHCl_3$), along with bromodichloromethane ($CHCl_2Br$), dibromochloromethane ($CHClBr_2$), and bromoform ($CHBr_3$), form a group of compounds known as the trihalomethanes (THMs). These compounds have been identified as major by-products of water disinfection processes involving chlorine. Over the last 10 years, there has been considerable interest in whether chlorination disinfection by-products (DBPs) in drinking water such as the THMs are associated with adverse birth outcomes (Nieuwenhuijsen et al. 2000a). A number of epidemiologic studies have been carried out on the association of DBPs with adverse birth outcomes, and we are currently conducting an association study in the United Kingdom (Toledano et al. 2001). Many of these studies assign an ecologic estimate of average THM concentrations as a marker for DBPs. Our U.K. study, for example, uses quarterly mean THM tap concentrations of water supply zones (areas defined for routine monitoring purposes in which fewer than 50,000 people reside) estimated from routinely collected data provided by the water suppliers (Whitaker et al. Unpublished data).

Exposure to volatile compounds such as THMs in drinking water occurs through multiple routes and pathways and varies from person to person depending on the individual's water usage; exposure to other nonvolatile DBPs such as the haloacetic acids is primarily through ingestion (Nieuwenhuijsen et al. 2000b). Routes of exposure to volatile compounds are ingestion, dermal absorption, and inhalation, and pathways can include any activity involving chlorinated water, such as ingestion of tap water, swimming, bathing, and showering. For example, an individual residing in an area with water with a low THM concentration may experience a relatively high level of exposure by attending a swimming pool, taking many long baths, or by drinking water with a high THM concentration outside the home.

Inaccurate and imprecise exposure estimates in epidemiologic studies may lead to loss of power and precision, and attenuation in health risk estimates (Armstrong 1998). The extent to which this happens depends on the relation between the exposure index that is used and the "true exposure," which in this context is the relation between the mean chloroform concentration of the water zone in which a mother resides and her average uptake of chloroform, respectively.

A number of studies have measured an individual's uptake of DBPs from various activities, using biologic markers such as breath samples, blood plasma samples, and urinary excretion rates (Nieuwenhuijsen et al. 2000b). Chloroform concentrations measured in breath or blood after swimming and showering have been found to be correlated with chloroform concentrations in the water and air (Aggazzotti et al. 1990, 1995; Jo et al. 1990; Lévesque et al. 1994; Weisel et al. 1999) and to increase with the time spent on the activity (Aggazzotti et al. 1990, 1995; Gordon et al. 1998; Lévesque et al. 1994).

In this article we present data from a simulation study to assess the relation between chloroform concentrations in the water supplied to the home, using the water chloroform concentrations estimated for each water supply zone in the U.K. epidemiologic study (Whitaker et al. Unpublished data), and chloroform uptake, taking into account chloroform-related activities. The study focuses only on chloroform—the most prevalent THM—and includes the most important water-use activities: showering, bathing, swimming, and ingestion of tap water. Uptake of chloroform was simulated based on information in the published literature about frequency and duration of each activity, amount of water ingested, and measured increases in blood chloroform concentrations. Results of the simulation study were used to evaluate the relation between our exposure index (the water zone mean chloroform concentration) and the assumed "true" exposure (the simulated chloroform uptake) and so inform on the level of measurement error in the exposure assessment for our epidemiologic study.

Methods

The etiologically relevant exposure period for a mother in epidemiologic studies of DBPs has been taken to be the last trimester (3 months) of pregnancy for birth weight and stillbirth, and the first trimester of pregnancy for congenital malformations (Nieuwenhuijsen et al. 2000a). Therefore, 90 days of chloroform uptake via showering, bathing, ingestion of tap water, and swimming were simulated for each mother and then averaged to give an average daily uptake for all pathways. Our epidemiologic study population includes mothers supplied with water from three U.K. water suppliers. Mean chloroform concentrations for each water zone within each supplier's region

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